

WHAT IS CLAIMED IS:

1. A high throughput screening apparatus for ultra high throughput screening of chemical compounds for a biological target, comprising a substrate having a plurality of channels, wherein each of said channels has a first end at a first face of the apparatus and wherein each of said channels has a second end, each said first end being one of a plurality of first ends and each said second end being one of a plurality of second ends, wherein the first ends of said channels are secured to a plurality of reaction chambers such that at least one of said first ends is in fluid communication with a different reaction chamber from at least one other of said first ends.

2. A high throughput screening apparatus according to claim 1, wherein said reaction chamber forms a portion of said first end.

3. A high throughput screening apparatus according to any of claims 1-2 wherein said reaction chamber is defined by a hydrophilic region at the first face of said apparatus surrounded by a hydrophobic region at the first face of said apparatus.

4. A high throughput screening apparatus according to claim 1 wherein each said reaction chamber is defined by a hydrophilic region at the first end of the channel corresponding to the reaction chamber and is further defined by a hydrophobic region surrounding the hydrophilic region at the first end of the channel.

5. A high throughput screening apparatus according to claim 1, wherein each of said first ends has an individual reaction well forming said reaction chamber, the

reaction well having a cross-sectional area that is greater than a cross-sectional area of its corresponding channel.

6. A high throughput screening apparatus according to claim 5, wherein said reaction well has an inner cross-sectional area and said channel has an inner cross-sectional area and wherein the inner cross-sectional area of said reaction well is no less than 5 times larger than the inner cross-sectional area of said channel.

7. A high throughput screening apparatus according to any of claims 5-6 wherein said reaction well is defined by a hydrophilic region on the first face of said apparatus surrounded by a hydrophobic region on said first face.

8. A high throughput screening apparatus according to any of claims 1-7, wherein each said second end is individually positionable.

9. A high throughput screening apparatus according to claim 8, wherein each said second end is individually attached to a corresponding through-channel of a plate configured to fit a microtiter plate such that each through-channel of the plate corresponds to an individual well of the microtiter plate.

10. A high throughput screening apparatus according to any of claims 1-7, wherein each said second end is positioned at a second face of the apparatus.

11. A high throughput screening apparatus according to claim 10 wherein the channels have a volume such that only one assay is performed using the apparatus.

12. A high throughput screening apparatus according to claim 10 wherein said apparatus has a first metering section and a second metering section, the first metering section comprising a channel of said channels wherein said channel is configured to draw a desired volume of a target liquid into the channel by capillary force, and the second metering section comprising a well on said second surface, the well being formed by a hydrophilic area and a hydrophobic area placed around an entrance to the channel such that a droplet of a second liquid of a desired volume forms when the second liquid is placed on said second surface.

13. A high throughput screening apparatus according to claim 10 wherein the apparatus has a length less than 50 cm.

14. A high throughput screening apparatus according to claim 13 wherein the apparatus has a length less than 10 cm.

15. A high throughput screening apparatus according to claim 13 wherein the apparatus has a length less than 1 cm.

16. A high throughput screening apparatus according to any of claims 10-15 wherein said channels have hydrophobic portions along a length of each of the channels such that fluid entering the channels by capillary action stops at the hydrophobic portions.

17. A high throughput screening apparatus according to any of claims 10-16 wherein each of said channels has a portion having a length and a cross-sectional area selected to provide a desired amount of a fluid when said fluid enters said channels through capillary action.

18. A high throughput screening apparatus according to any of claims 10-17 wherein the reaction chamber is lined with a reflective material.

19. A high throughput screening apparatus according to any of claims 10-18 wherein each second end forms a well having a cross-sectional area greater than a cross-sectional area of the channel.

20. A high throughput screening apparatus according to any of claims 1-19 and further comprising a first removable sealant upon said first face.

21. A high throughput screening apparatus according to any of claims 1-20, wherein the apparatus has at least about 500 channels per cm<sup>2</sup> as measured at the first ends of the channels.

22. A high throughput screening apparatus according to any of claims 1-21, wherein each channel has a wall that is sufficiently hydrophilic and an inner diameter that is sufficiently small such that a liquid is retained within the channel by capillary force.

23. A high throughput screening apparatus according to any of claims 1-22, wherein the high throughput screening apparatus has at least 100 channels.

24. A high throughput screening apparatus according to claim 23, wherein the high throughput screening apparatus has at least 500 channels.

25. A high throughput screening apparatus according to any of claims 1-23, wherein said first ends are secured to one another in a solid mass such that the first ends are substantially coplanar in a static array in a facet of the solid mass.

26. A high throughput screening apparatus according to any of claims 1-25, wherein said apparatus is formed of a bundle of a plurality of capillaries.

27. A high throughput screening apparatus according to claim 26, wherein said capillaries comprise light-conducting capillaries.

28. A high throughput screening apparatus according to any of claims 1-27, wherein each of said channels contains a distinct probe in solution.

29. A high throughput screening apparatus according to claim 1-27, wherein each of said channels contains a distinct probe attached to a wall of each of said channels.

30. A high throughput screening apparatus according to any of claims 28-29, wherein each of said probes is selected from a group consisting of deoxyribonucleic acids (DNA), ribonucleic acids (RNA), synthetic oligonucleotides, antibodies, proteins, peptides, lectins, modified polysaccharides, synthetic composite macromolecules, functionalized nanostructures, synthetic polymers, modified/blocked nucleotides/nucleosides, modified/blocked amino acids, fluorophores, chromophores, ligands, chelates, haptens and drug compounds.

31. A high throughput screening apparatus according to claim 30, wherein the probe comprises a tyrosine kinase protein selected from the group consisting of epidermal growth factor receptor (EGFR), platelet-derived growth factor receptor (PDGFR), fibroblast growth factor receptor (FGFR), colony stimulating factor-1, (CSF-1), insulin receptor, phospholipase C- $\alpha$  (PLC- $\alpha$ ) and insulin like growth factor-1 (IGF-1)

32. A high throughput screening apparatus according to any of claims 28-31, wherein said probe is coupled to a bead.

33. A high throughput screening apparatus according to any of claims 28-31, wherein the probe is in a solution phase.

34. A high throughput screening apparatus according to any of claims 28-31, wherein the probe is in a colloidal dispersion.

35. A system for providing a combinatorial library, said system comprising a high throughput screening apparatus according to any of claims 1-27 and a fluid delivery system comprising a filling tube having a size suitable to fill a channel of the high throughput screening apparatus.

36. A system for providing a combinatorial library, said system comprising a high throughput screening apparatus according to any of claims 1-7 and 10-27 and a fluid delivery system comprising a plurality of capillaries having first ends positioned so that said first ends match with the second ends of the channels of the high throughput screening apparatus.

37. A system according to claim 36, wherein the first ends of the capillaries of the delivery system are in a capillary face that fits against the first face of the high throughput screening apparatus.

38. A desktop screening system comprising a system according to any of claims 35-37 and a detector that detects a signal indicative of an interaction between a probe and a target.

39. A method of fabricating a high throughput screening apparatus comprising

(a) forming a substrate having channels that terminate in a first face;  
and

(b) forming a plurality of reaction chambers at the first face such that at least one of said channels is in fluid communication with a different reaction chamber from at least one other of said channels.

40. A method according to claim 39 wherein the act of forming a plurality of reaction chambers provides that each of the channels terminates individually at a reaction chamber of said plurality.

41. A method according to any of claims 39-40 wherein said reaction chamber comprises a virtual well formed by a hydrophilic region on the first face immediately adjacent to an individual channel, which hydrophilic region is surrounded by a hydrophobic region.

42. A method according to claim 41 wherein said virtual well is formed by applying a mask to the first face and exposing an unmasked portion of the first face to energy sufficient to cleave a cleavable portion of a molecule attached to the first face.

43. A method according to any of claims 39-42 wherein the act of forming a substrate having said channels comprises forming a bundle of capillaries so that said channels of the capillaries terminate in said first face.



44. A method according to claim 43 and further comprising forming said bundle of capillaries such that said channels of the capillaries terminate in a second face.

45. A method according to claim 44 and further comprising forming a virtual well around each channel at said second face by providing a hydrophilic region on the second face immediately adjacent to said channel and surrounding said hydrophilic region with a hydrophobic region.

46. A method according to claim 45 wherein said virtual well is formed by applying a mask to the first face and exposing an unmasked portion of the first face to energy sufficient to cleave a cleavable portion of a molecule attached to the first face.

47. A method according to claim 44 and further comprising forming a physical well at each channel at said second face by providing an opening at said second face having a cross-sectional area greater than a cross-sectional area of the channel.

48. A method according to claim 47 wherein said physical well is formed by etching the substrate.

49. A method for fabricating an array according to claim 3 or claim 7, the method comprising applying a mask to define the hydrophilic zone and the hydrophobic zone.

50. A method of metering a volume of a liquid comprising placing a first liquid having a surface tension suitable to form a droplet of predetermined volume in a hydrophilic region and a hydrophobic region of a substrate, which hydrophobic region surrounds said hydrophilic region, and removing the first liquid from the hydrophobic region.

51. A method according to claim 50 wherein the substrate has a channel that opens to the hydrophilic region of the substrate, and wherein the channel has been filled with a second liquid prior to placing the first liquid in the hydrophilic region and the hydrophobic region.

52. A method according to claim 51 wherein the channel has a cross-sectional area and length to provide a predetermined volume of the second liquid within the capillary.

53. A method according to claim 52 wherein the method further comprises moving both the first liquid and the second liquid through the channel and into a reaction chamber.

54. A method according to claim 53 wherein the reaction chamber forms a portion of the substrate.

55. A method for determining an affinity of a compound for a receptor, the method comprising:

- (a) immobilizing the receptor on a wall defining a channel of an array of channels;
- (b) binding to the receptor a saturating amount of ligand specific for the receptor;
- (c) contacting the array with an excess of said compound; and
- (d) measuring a rate of displacement of bound ligand by the compound.

56. A method according to claim 55 wherein the array of channels comprises a capillary array, and the wall defining said channel comprises a capillary.

57. A method according to claim 56 wherein the capillary is an optical fiber capillary and the act of measuring the rate of displacement comprises measuring the rate of displacement of bound ligand by the compound by monitoring an intensity of light conveyed by the optical fiber capillary.

58. A method according to any of claims 55-57, further comprising:

- (a) removing unbound ligand and compound from the channel;
- (b) introducing an acid plug into the channel to elute all bound ligand and compound into the acid plug; and

(c) measuring a signal indicative of the ligand and compound, wherein at least one of the ligand and the compound is coupled to a moiety that produces a detectable signal.

59. A method for determining an affinity of a compound for a receptor, the method comprising:

- (a) immobilizing the receptor on a wall defining a channel of an array of channels;
- (b) binding to the receptor a mixture of a saturating amount of a ligand specific for the receptor and a saturating amount of a compound; and
- (c) measuring a ratio of bound ligand to bound compound.

60. A method according to claim 59, wherein the array of channels comprises a capillary array, and the wall defining said channel comprises a capillary.

61. A method according to claim 60 wherein the capillary is an optical fiber capillary and the method further comprises measuring the ratio of bound ligand to bound compound by monitoring light conveyed by the optical fiber capillary.

62. A method according to any of claims 59-61, further comprising:

- (a) removing unbound ligand and compound from the channel;
- (b) introducing an acid plug into the channel to elute all bound ligand and compound into the acid plug; and

(c) measuring a signal indicative of the ligand and compound, wherein at least one of the ligand and the compound is coupled to a moiety that produces a detectable signal.